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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/618,288	04/25/2003	Thomas E. Barta	00988/1/US (6794-000053/U)	7868
28880	7590	07/14/2005	EXAMINER	
WARNER-LAMBERT COMPANY 2800 PLYMOUTH RD ANN ARBOR, MI 48105			BERNHARDT, EMILY B	
			ART UNIT	PAPER NUMBER
			1624	

DATE MAILED: 07/14/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/618,288

Applicant(s)

BARTA ET AL.

Examiner

Emily Bernhardt

Art Unit

1624

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 04 May 2005.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-374 is/are pending in the application.
- 4a) Of the above claim(s) See Continuation Sheet is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1,2,8,10,15,19-21,26,43,45-50,61,62,64,66,74-76,79 and 374 is/are rejected.
- 7) ☒ Claim(s) 77 and 78 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date 9/25/03 & 1/31/05
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____

Applicant's election without traverse of Group I and subgroup B in the reply filed on 5/4/05 is acknowledged. For the record claims 15 and 36 should have been included in Group I. However, in view of the many differing species present within Group IB which are variously classified as set forth in the previous action, based on species elected (76-11), corresponding "E1" ring as pyridyl will be held as constructively elected. The claims which read on this subject matter are: 1,2,8,10,15,19-21,26,43,45-50,61-62,64,66,74-79 and 374. Note that claim 63 is not included in the above set since E1 in this claim appears to be directed to saturated hetero rings. Applicants are advised that the claims will only be examined with respect to the elected subject matter, namely A1/A2 as forming hetero rings, Y=N and E1 as pyridyl.

Claim 48 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

1. Claim 48 recites for R^x "aldehydo" which is not an art-recognized moiety but rather a class of compounds, namely aldehydes. Thus it is not known how such is attached to the remainder of the compounds or structural makeup. Also, antecedent basis for this term is not seen in claim 43 from which 48 depends.

Claims 1,2,8,10,15,43,45-50 and 374 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for A1/A2 rings of the scope permitted in claim 19, does not reasonably provide enablement for any and all heterocyclic rings as embraced by the broader generic claims . The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims. From a reading of the specification the scope of A1/A2 can entail any hetero ring regardless of size and degree of unsaturation as well as point of attachment to the sulfonyl group and be further substituted with an array of functional groups. While many compounds have been made and tested these are consistently piperidino or pyrano substituted at the 4-position with the sulfonyl moiety. There is thus no reasonable assurance as to what other rings will work. Note In re Surrey 151 USPQ 724 regarding sufficiency of disclosure for a Markush group where as herein no examples of a diverse nature have been made much less tested showing the requisite activity needed to practice the invention. Also see MPEP 2164.03 for enablement requirements in cases directed to structure-sensitive arts such as the pharmaceutical art. Also note the criteria for enablement as set out

in *In re Wands* cited in MPEP 2164.01(a), August 2000 edition, which includes factors such as:

- 1) Breadth of the claims- the claims cover compounds easily in the millions;
- 2) Level of unpredictability in the art- the invention is pharmaceutical in nature involving inhibitory activity at one or more MMP receptors. It is well established that “the scope of enablement varies inversely with the degree of unpredictability of the factors involved” and physiological activity is generally considered to be unpredictable. Applicants’ own test data confirms this. See *In re Fisher* 166 USPQ 18;
- 3) Direction or guidance- as stated above A1/A2 compounds actually made are much closer to each other than to remaining scope ;
- 4) State of the prior art- The compounds are sulfamato hydroxamic acid derivatives. Such compounds having this feature are also known in the art with similar rings as that exemplified herein.
- 5) Working examples- While test data has been presented it is limited to 2 types of rings as discussed above and thus no clear evaluation of what other type of rings out of the many claimed might affect potency to a large or small degree.

In view of the above considerations, this rejection is being applied.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1,2,8,10,15,19-21,26,43,45-50,61-62,64,66,74-76,79 and 374 are rejected under 35 U.S.C. 103(a) as being unpatentable over DeCrescenzo (US'250 or WO'221, both cited by applicants). US'250 is applied as of its earlier provisional filing date of 2/8/99 and WO'221 was published more than a year earlier of applicants' earliest filing date. The reference describes many compounds with substituents thereon that are also exemplified herein for use as metalloprotease inhibitors. See Formula I which permits piperazine as $\text{NR}^{3a}\text{R}^{3b}$ with heteroaryls such as pyridine directly attached and which in turn can be further substituted with groups such as alkyl, alkoxy, haloalkyl and aryl. See cols 13-18 in the US patent and pages 9-22 in the WO publication. While examples such as egs.10,32,33,37,38,53 and 55 do not anticipate the instant scope they are very structurally similar being substituted with phenyl in place of pyridyl. However DeCrescenzo clearly teaches pyridyl as a choice on $\text{NR}^{3a}\text{R}^{3b}$ rings as can be seen in the many species exemplified for other $\text{NR}^{3a}\text{R}^{3b}$ rings. See cols. 42,43,98,164,260

and 383 which show point of attachment at all ring positions. While species in claims 76 and 79 have additional substituents on either A1/A2 ring and/or pyridine ring, these substituents have been contemplated by the prior art as well. For example for the elected species (76-11) in claim 76 which has a methoxy on pyridyl ring see methoxy substituted phenyl derivatives in cols.216,262 and 385. Compare (76-24) in claim 76 with eg.32 in DeCrescenzo- the sole difference being 2-pyridyl in place of phenyl. In claim 79 (79-1) is similar to eg.32 but also has a pyrimidyl on piperidino nitrogen of A1/A2. Note this feature is also exemplified in eg.22 and in other species. Compound (79-7) in claim 79 is very close to eg.38, claim 6 in DeCrescenzo- the sole difference being 2-pyridyl in place of phenyl. Thus it would have been obvious to one skilled in the art at the time the instant invention was made to replace phenyl rings in piperazino species pointed out above with pyridyl and optionally further substitute said ring as well A1/A2 ring with moieties exemplified in many other embodiments of DeCrescenzo's disclosure with the expectation that such resulting compounds will also have metalloprotease activity in view of the equivalency teachings outlined above.


Claims 77 and 78 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims. The substitution on

pyridyl in these species is not particularly suggested by DeCrescenzo, the closest art found.

Applicants' IDS statements have been reviewed. Most have been completely considered by the examiner. However, for IDS filed 9/25/03, foreign refs.23-36 are not seen in the file. For other IDS statements which list copending applications, while these have been seen by the examiner, they need to be inserted into "Other Documents" section in compliance with MPEP 609. Once resubmitted they will be indicated as considered.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Emily Bernhardt whose telephone number is 571-272-0664.

If attempts to reach the examiner by telephone are unsuccessful, the acting supervisor for AU 1624, James O. Wilson can be reached at 571-272-0661. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.


EMILY BERNHARDT
PRIMARY EXAMINER
GROUP 1600

Continuation of Disposition of Claims: Claims withdrawn from consideration are 3-7,9,11-14,16-18,22-25,27-42,44,51-60,63,65,67-73 and 80-373.